A Descriptive Anatomy of the Face in Human Fetuses with Unilateral Cleft Lip and Palate

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This study describes the morphology of the facial bones and cartilages in fetuses with a unilateral cleft of the lip and palate. The face affected by a unilateral cleft presents at birth certain deviations which are extremely consistent from case to case. The purpose of this paper is to try to establish when these deviations arise and to determine whether they become progressively more severe during fetal life.

The unilateral cleft is in some respects an experiment on the growth of the face. The cleft separates the maxillary bone from structures which directly or indirectly may influence its development. In this study the size and position of the maxilla on the cleft side was compared with that on the opposite side.

Review of the Literature

There is extensive literature regarding the normal development of the bones of the face. Papers by Noback and Moss (*8*), Woo (*11*), and Chase (*3*) discuss the early development of the facial bones. Kraus (*4*) has considered the development of the palate in more detail. The non-cleft skull at certain ages has been meticulously described by earlier investigators, for example, Macklin (*6*, *7*).

Because of the rarity of cleft palate fetal material, there have been relatively few publications relating to the morphology of such facial structures. Kraus, Kitamura, and Latham (*5*) have produced an atlas of embryology in which the histology of cleft specimens is compared to normal. Stark (*9*) describes three unilateral cleft palate embryos and finds that there is a mesodermal deficiency on the cleft side in the region of the primary palate, which he regards as a possible factor in the etiology of cleft of the primary palate. Avery (*2*) finds defective cartilage formation in cleft fetuses.

Method

The cleft specimens used in this study are described in Table 1, together with the crown-rump length and age. Fifteen cleft specimens

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TABLE 1. Description of 15 specimens for study. Specimens with the X prefix had a cleft of the primary palate only.

Specimen	*CR length*	*Estimated age*	*Preparation*
3596	37 mm	60 days	embedded
W 50	39 mm	9 weeks	sectioned
2448	51 mm	10 weeks	sectioned
2730	52 mm	10 weeks, 3 days	embedded
3196	59 mm	11 weeks	embedded
3080	71 mm	11 weeks, 1 day	embedded
2336	75 mm	12 weeks	sectioned
X2464	137 mm	16 weeks	sectioned
2812	164 mm	17 weeks, 5 days	sectioned
W85	176 mm	19 weeks	sectioned
4258	197 mm	23 weeks	macerated
V11		36 weeks	dried skull
X4107		38 weeks	macerated
V10		40 weeks	dried skull
V12		40 weeks	dried skull

were available for study and preparation. No vital information was obtainable on any of them. The fresh specimens were aborted fetuses, fixed in formalin in various states of preservation. The fertilization age was obtained by measuring the crown-rump length and weight and comparing the measurements to the growth curve of Streeter (*10*). Three specimens were fetal skulls examined by the kind permission of the Museum Vrolik, Amsterdam.

Three sets of specimens were studied by gross morphological technique: a) The heads of a noncleft series of fetuses (7 to 14 weeks) were macerated, stained with alizarin red S, cleared, and embedded in bioplast. The method used was that previously described by the author (*1*), modified by the substitution of xylene and bioplast (Wards) for acetone and bakelite. The heads of the four cleft specimens were prepared by the same technique. b) Specimen 4258 (24-weeks) and specimen 4107 (38-weeks) were macerated and preserved in 70% alcohol. c) Three dried skulls were examined at the Museum Vrolik.

In addition, histological technique was used to study normal and cleft palate specimens from the collection of fetal material in the museum of the Cleft Palate Research Center, University of Pittsburgh. These specimens had been photographed and then sectioned in the coronal plane.

Measurements

Measurements were taken on the cleft and noncleft specimens to express the relationship between the width of the palate and age. The width was taken as the distance between the inner alveolar walls at the level of the posterior margin of the bony maxillary shelf. The age was plotted against width of palate in the form of a scatter diagram (Figure

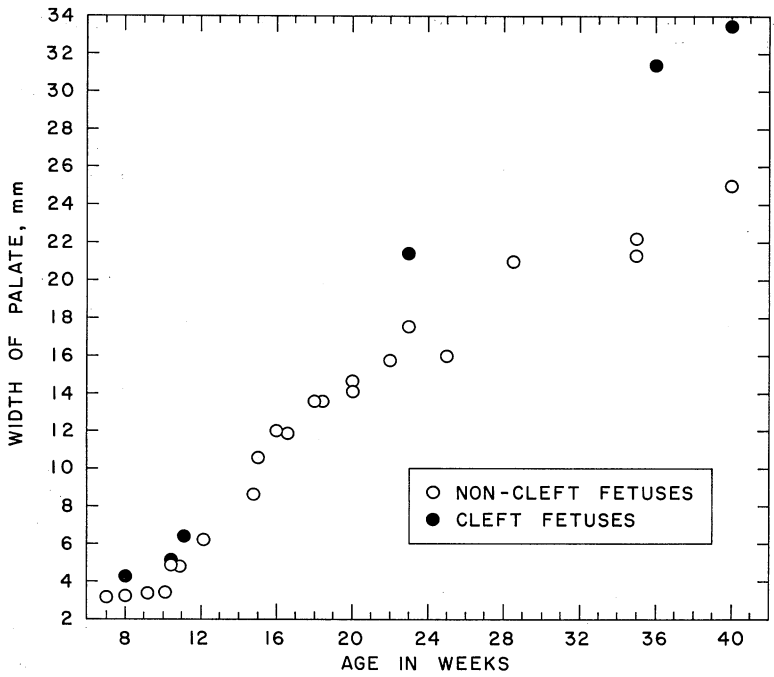

FIGURE 1. Scatter diagram showing the relationship between age of fetus (in weeks) and width of palate (in mm).

1). The length of the palate was also plotted against age (Figure 2). The length was measured from the most anterior point on the alveolar margin to the level of the junction of the posterior margin of the bony palatal shelf with the palatine bone. The noncleft side only was measured on the cleft specimens.

Figures 1 and 2 show that width is greater in the cleft specimens, but that length appears similar for the two groups.

In order to measure the effect of the cleft on the growth of the maxilla on the cleft side, the size of this bone on the cleft side was compared with that on the noncleft side. Measurements were taken from a) the posterior margin of the canine crypt to the posterior margin of the inner alveolar wall and from b) the posterior margin of the canine crypt to the posterior margin of the zygomatic process. These measurements, as well as the percentage ratio of the cleft side to the noncleft side of these measurements, are shown in Table 2.

Table 2 shows that the maxilla was smaller on the cleft side than on the noncleft side on the first measurement (canine crypt to the posterior margin of the minor alveolar wall) and that difference was significant.

The youngest specimen examined for this study (specimen 3596) was 60 days old (CR 37 mm). It presented a complete cleft of the left side. The condition of the specimen was good. It was embedded in bioplast

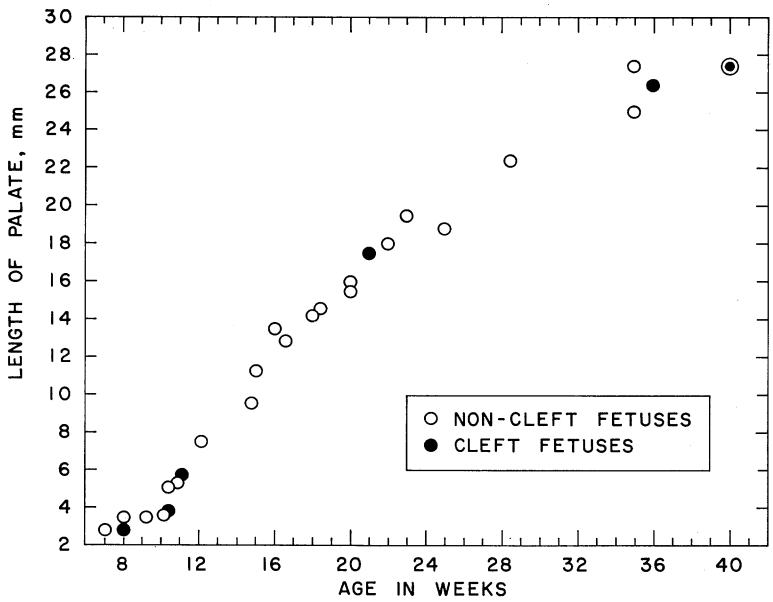

FIGURE 2. Scatter diagram showing the relationship between age of fetus (in weeks) and length of palate (in mm).

TABLE 2. The length, in mm, of the maxillae in the cleft specimens as measured from the canine crypt to the posterior border of the maxilla and the zygomatic process. Also reported are ratios between the cleft side length and the concleft side, expressed as a percentage.

Specimen	*Canine crypt to alveolus*			*Canine crypt to zygomatic*		
	cleft side	*noncleft*	%	*cleft side*	*noncleft*	%
3596	0.98	1.03	95	1.51	1.63	93
2730	2.55	2.45	104	2.85	2.56	111
3196	2.61	3.09	84	3.29	3.28	100
3080	2.91	3.46	85	4.00	4.21	95
4258	10.1	11.3	90	9.8	9.4	104
V10	16.6	17.5	95	14.5	14.5	100

and examined microscopically. Drawings of the palate of this specimen and of a control normal (CR 35) were made using a Camera Lucida microscope at a magnification of 12.3 (Figure 3).

The cleft specimen showed a marked shift of the premaxillary region away from the center line, towards the noncleft side. A wide cleft separates the premaxillary region of the cleft side from the maxillary region. The premaxilla of the cleft side is reduced in size and is displaced forward. The premaxilla (taken as the area of bone anterior to the canine crypt) of the cleft specimen is smaller on the noncleft side

FIGURE 3. Drawings of specimen 3596, left, and a noncleft fetus, right, at the age of 60 and 56 days, respectively (drawn by Mr. Q. Beery).

than is the premaxilla of the control specimen. The spicules of bone are directed at right angles to the midline suture in the noncleft specimen, but in the cleft specimen they lack this orientation. This was interpreted as being due to a lack of tension across this suture.

On the cleft side the maxilla closely resembles the appearance of the bone on the noncleft side (excluding the premaxillary region). The palatine bones are similar on each side. Measurements made with a veneer attachment to the microscope show the maxilla on the cleft side to be smaller than that on the noncleft (Table 2). Even at this early stage the bony palatal shelves of the maxilla and palatine bones show some lack of growth and the bone spicules present a less open pattern than in the control specimen.

The vomer bone appears to be developing normally at this stage.

The width of the palate is greater than in the control specimens in the eighth and ninth weeks (Figure 1).

The cartilage of the nasal septum can be seen faintly under the microscope. It appears to be vertical except in the anterior region where it curves laterally to the area between the premaxillae, which will become the anterior nasal spine.

Figure 4 shows the palatal aspect of an 11-week cleft specimen (specimen 3080), and a control specimen of the same age. The specimen had a complete unilateral cleft, and also a small Simonart's bar. The premaxillary region is displaced laterally. The premaxilla on the cleft side is much reduced in size. There also appears to be reduction in the size of the premaxilla on the noncleft side. The vomer bone now presents a marked swing of the lower anterior part towards its articulation with the bony palate. The maxilla on the cleft side is retroplaced in relation to the noncleft side. It resembles the noncleft side of the maxilla in form but is slightly smaller (Table 2). The bony palatal shelves now show a marked reduction in size, the cleft side being the more severely affected.

From the frontal aspect (Figure 5), the nasal bones show a deviation in form characteristic of the unilateral cleft, but not as marked as in older specimens. The shift of the suture between the premaxillary bones away from the center line is well shown.

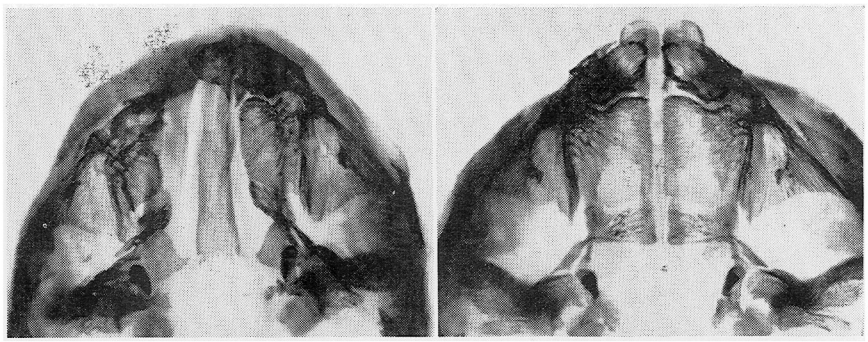

FIGURE 4. The palatal aspect of the face of 11-week specimen 3080, left, and a noncleft fetus, right.

FIGURE 5. The frontal aspect of a cleft and noncleft, same specimens as in Figure 4. Specimen 3080, left, and a noncleft fetus, right.

Specimens 4258, V10, and V11 range in age from 24 weeks to birth. The general appearance of the specimens is very similar. They were all complete unilateral clefts; specimens 4258 and V10 were cleft on both sides of the secondary palate also (Figure 6). The features described for the previous specimen are all present in these. The nasal bones now show a marked distortion and the frontal process of the maxillae are also affected. The nasal bone and frontal process of the maxilla on the cleft side shows what might be described as a flattening, while on the noncleft side the bones are more curved. The depth of the nasal aperture appears less high than in noncleft specimens.

Histological Appearance

Deviations in the bones and cartilages of the specimens prepared histologically can be seen at all ages. Specimens 2812 and W85 closely resemble each other and will be described first. The cartilage of the nasal capsule in these specimens is well developed and differs from control specimens in form rather than in any failure of development.

The nasal septum shows a bend in the lower anterior part towards

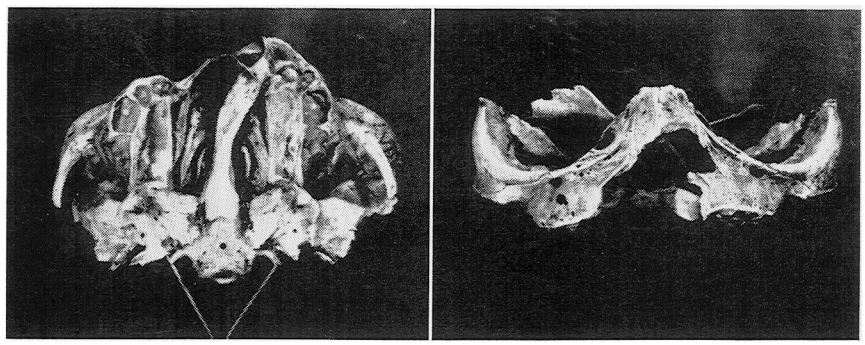

FIGURE 6. The palatal left, and frontal, right, aspects of 36-week cleft fetus (specimen V 10).

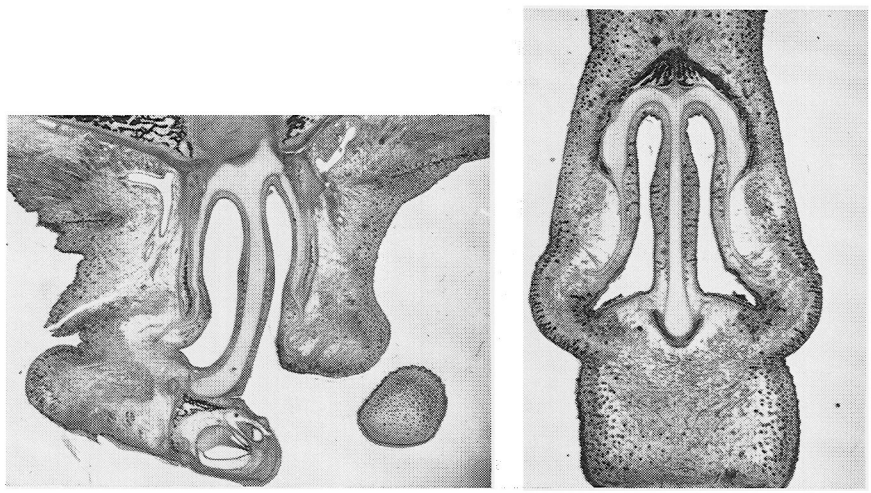

FIGURE 7. Coronal sections through the region of the anterior nasal spine of cleft fetus specimen 2812, left, and a noncleft 17-week-old fetus, right.

the anterior nasal spine region which, as observed above, is laterally placed (Figure 7). When the nasal septum is traced posteriorly, it rapidly assumes a more upright position (Figure 8). The body of the nasal septum maintains a slight curve for much of its length so that it lies nearer the conchae and nasal walls of the noncleft side (Figure 9). Immediately posterior to the anterior nasal spine, the paraseptal cartilages make their appearance. In normal specimens, these are disposed vertically alongside and below the nasal septum. In cleft specimens, the paraseptal cartilages are almost horizontally disposed, extending from the lower border of the nasal septum, which is becoming more upright, to the premaxilla on the noncleft side (Figure 8). The paraseptal cartilages thus participate in the formation of the palate. Some distortion of the alar cartilages can be seen. The alar cartilage on the cleft side

FIGURE 8. Coronal section through the premaxilla of the same specimens (cleft, left; noncleft, right). These sections are at the point of maximum formation of the paraseptal cartilages.

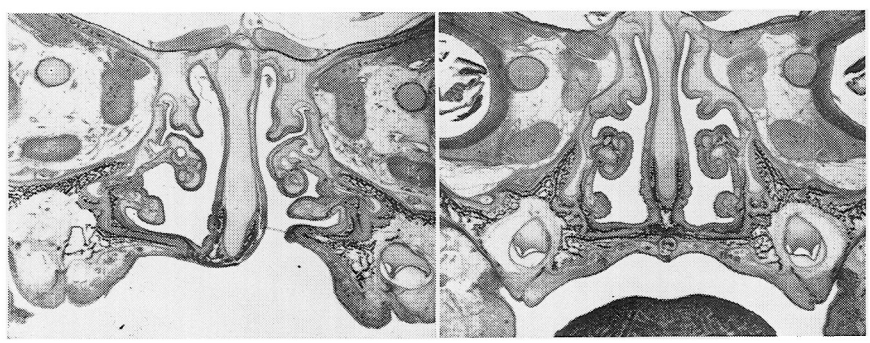

FIGURE 9. Coronal sections through the maxilla of the same specimens in Figure 7 (cleft, left; noncleft, right). These sections pass through the second deciduous molar, and the region of the palatal shelf where the bony shelf of the palatine bone overlaps that of the maxilla.

lacks the curve of its lower margin; this corresponds to the clinical observation of a normal alar base on the noncleft side and a 'taut' appearance on the cleft side.

As might be anticipated from the microscopic appearance, deficiencies in the bones of these specimens appear in the region of the premaxilla and palatal shelves. The premaxilla on the cleft side forms little more than the crypt for the developing tooth germs. The premaxillae extend posteriorly as the intervomerine process. This process develops on the inner aspect of the paraseptal cartilage. In the cleft specimens, the intervomerine processes are horizontally disposed on the inner aspect of the paraseptal cartilages (Figure 8).

The maxillary bones are similar on each side. They appear wider apart than in the normal specimen. The nasal cavity is shorter and more widely based than in the noncleft (Figure 9). The walls, particularly below the level of the middle nasal conchae, slope outward more than in the noncleft. The palatal shelves are at the level of the lower border of the nasal septum whereas, in the noncleft, they are below this level. The shelves are reduced in width, the shelf on the cleft side showing more reduction than on the noncleft. The vomer is markedly deviated in its lower border. This part, which is normally vertically disposed, is horizontal in the cleft specimens and articulates directly with the bony palate.

The palatine bones are affected in the region of the shelves which, like the bony maxillary shelves, show a reduction in development. They are directed in a horizontal and an upwards direction.

Similar deviations in the forms of the bone and cartilages are seen in younger specimens. Specimen 2336, aged 12 weeks, shows a massive curve in the lower anterior part of the nasal septum. The paraseptal cartilages are horizontally disposed. Specimen W50, aged 9 weeks, shows a deviation in the septum but not in the paraseptal cartilages.

Discussion

It is apparent from the examination of these specimens that many of the features which characterize the unilateral cleft palate face are present at an early stage of fetal development. The displacement of the premaxillary region laterally, away from the center line, is present in all specimens and is well shown in the youngest plastic-embedded specimen (aged 8 weeks). Associated with this is the curve of the lower anterior part of the nasal septum which deviates laterally towards the anterior nasal spine. The maxillary bodies are wider apart than in the control specimens and are almost equidistant from the midline. A slight retroplacement of the cleft side is present in the well-preserved specimen 3196 (aged 11 weeks). This feature is noticeable in subsequent specimens. The bony palatal shelves of both sides and the premaxilla on the cleft side are reduced in development throughout. The features described above are present to approximately the same degree throughout the period studied. It seems probable that the bone, and possibly the cartilage, are laid down in mesoderm in a position which deviates from the normal and that this abnormal pattern tends to persist.

The unilateral cleft separates the maxilla from structures with which it would normally be in continuity. However, the cleft appears to have little effect on the growth of the maxillary bone on the cleft side when compared with the noncleft side. This bone is only slightly smaller than the noncleft maxilla as measured from the posterior border of the canine crypt to the posterior margin of the inner alveolar wall (a mean reduction of 8%). The dimension of canine crypt to zygomatic process appears unaffected and the height as shown on the histological sections is similar. Certain areas are affected by the cleft.

The premaxilla on the cleft side is severely reduced in size. On the noncleft side, this bone also appears to suffer a reduction in development when compared with the control specimen. The lack of tension across the interpremaxillary suture may be the reason for the failure of this bone to achieve its full development. Similarly, the palatal shelf on the noncleft side is reduced in size for, although there is continuity of tissue between the palatal shelf and the vomer, the bony palate on the noncleft side grows only slightly more than on the cleft side.

The increase in width between the maxillary bones in the cleft specimens, as compared with the control series, is a noticeable feature of all but one specimen. The lateral displacement of the maxillary regions may be responsible for deviations in other structures. It contributes, along with the reduction in development of the premaxilla, to the deviation of the lower anterior part of the nasal septum. It is partially, if not completely, responsible for the lack of depth to the nasal cavity during foetal life.

The cartilages of the face in cleft-affected fetuses show a distortion rather than a deficiency of tissue. As shown histologically on coronal sections, the most striking feature is the characteristic bend in the anterior part of the nasal septum. This curves downwards and laterally to the anterior nasal spine and is clearly demonstrated in the older specimens. Unfortunately, however, the poor state of preservation of the cartilaginous tissue in specimens younger than the 9th week has precluded their use in this portion of the study. It seems probable, however, that the curve of the nasal septum would be found at a younger age. It is certainly apparent at 8 weeks in the embedded specimen 3596.

When the septum is traced posteriorly, it rapidly assumes a more upright position. The more upright position of the septum is associated with the appearance of the paraseptal cartilages which in the cleft specimens are horizontally disposed, extending, like the vomer, from the base of the septum to the maxilla. In the region of the concha, the nasal septum always lies nearer the cleft side than the noncleft side, so that the nasal passage is narrower than the cleft side. It appears to incline or bulge in that direction.

Summary

The morphology of the bones and cartilages of unilateral cleft palate fetuses has been described from the study of macerated, alizarin-stained specimens, and histologically prepared specimens. Certain features characteristic of the unilateral cleft are apparent as early as the 8th week of fetal life. There is a displacement of the premaxillary region laterally, away from the center line. The maxillae are wider apart than in the controls, and are symmetrically placed in relation to the midline. The lower anterior part of the nasal septum is deviated towards the laterally-placed anterior nasal spine. There is a reduction in the development of the premaxilla on the cleft side, the palatal shelves on

both sides, and, to a lesser extent, the premaxilla on the noncleft side. The pattern of development established at this age appears to persist throughout fetal life.

Although there is continuity of tissue between the noncleft side and the rest of the face, the effect of the cleft is remarkably similar on the two sides if the premaxillary regions are excluded. The size and form of the body of the maxilla on the cleft side closely resembles that on the noncleft side. There is, however, a small reduction in the length of the bone as measured from the canine crypt to the posterior border of the maxilla. Other dimensions appear the same. From the 11th week, at the least, the maxilla and palatine bones on the cleft side are slightly retroplaced in relation to the noncleft side.

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Acknowledgment: I am grateful to Dr. Van Limborgh and to the Museum Vrolik for the kind permission to use the three cleft skulls presented in this paper. Figure 6 was supplied by the Museum Vrolik.

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